

REMARKS

The present invention is directed to a method for isolating cells that express FLK-2 receptors on their surface. Claim 81 is currently pending.

Amendments to the Title

Applicants have amended the title to recite "Method For Isolating Cells Expressing Flk-2 Receptors."

Amendments to the Claims

Applicants have amended claim 81 to recite a method for isolating cells that express FLK-2 on their surface, the method comprising binding the cells to a polyclonal or monoclonal antibody specific for the extracellular portion of a protein tyrosine kinase that is FLK-2. The extracellular portion of FLK-2, as amended, is defined by amino acids 1-517 of SEQ ID NO:2 or 1-516 of SEQ ID NO:4, and isolating the cells that are bound to the antibody from cells that are unbound to the antibody.

Discussion of Office Action

In an Office Action dated June 2, 2003, the Office (i) requested priority information; (ii) required a new title; (iii) required formal drawings; (iv) required the review of SEQ ID NOs; (v) required the review of trademarks; (vi) rejected claim 81 as lacking adequate written description under 35 U.S.C. § 112, first paragraph; (vii) rejected claim 81 as not enabled under 35 U.S.C. § 112, first paragraph; (viii) rejected claim 81 as indefinite under 35 U.S.C. § 112, second paragraph; and (ix) rejected claim 81 as obvious under 35 U.S.C. § 103(a).

Priority Information

In response to the Examiner's request for priority information, Applicants submit that this application is a continuation of copending application U.S. Serial No. 09/208,786, filed December 10, 1998, which is a continuation of U.S. Serial No. 09/021,324 filed February 10,

Appl. No. 09/919,408
Amdt. dated Dec. 2, 2003
Reply to Office Action of June 2, 2003

1998, now U.S. Patent 5,912,133, which is a continuation of U.S. Serial No. 08/601,891 filed February 15, 1996, now U.S. Patent No. 5,747,651, which is a divisional of U.S. Serial No. 08/252,498 filed October 31, 1994, now abandoned, which is a divisional of U.S. Serial No. 08/055,269 filed April 30, 1993, now U.S. Patent No. 5,367,057, which is a divisional of U.S. Serial No. 07/977,451 filed November 19, 1992, now U.S. Patent No. 5,270,458, which is a continuation-in-part of U.S. Serial No. 07/975,049 filed November 12, 1992, now abandoned, which is a continuation-in-part of U.S. Serial No. 07/906,397 filed June 26, 1992, now U.S. Patent No. 5,621,090, which is a continuation-in-part of U.S. Serial No. 07/813,593 filed December 24, 1991, now U.S. Patent No. 5,185,438, which is a continuation-in-part of U.S. Serial No. 07/793,065 filed November 15, 1991, now abandoned, which is a continuation-in-part of U.S. Serial No. 07/728,913 filed June 28, 1991, now abandoned, which is a continuation-in-part of U.S. Serial No. 07/679,666 filed April 2, 1991, now abandoned.

For the convenience of the Examiner, copies of the specifications of US Application Nos. 07/679,666 and 07/728,913 are enclosed.

Amendments to the Title

As required by the Examiner, Applicants have amended the title to clearly indicate the claimed invention. Thus, the title is now descriptive of the claimed invention.

Formal Drawings

As required by the Examiner, Applicants resubmit the twenty-three (23) sheets of formal drawings, which, along with the formal drawings previously filed May 13, 2003 meet the formality requirements of 37 C.F.R. § 1.84.

Sequence Listings

As requested by the Examiner, Applicants have reviewed the SEQ ID NOs, which, in light of the Sequence Listings previously filed May 13, 2003, Applicants believe meet the requirements of 37 C.F.R. § 1.821-1.825.

Trademarks

As requested by the Examiner, Applicants have reviewed the application for all spelling, TRADEMARKS, and like errors, and Applicants believe no corrections are required.

Written Description

Claim 81 has been rejected under 35 U.S.C. § 112, first paragraph for failure to provide sufficient written description of the FLK-2 receptor. The Examiner explains that the specification needs to include “relevant identifying characteristics such as structure of other physical and/or chemical characteristics” to sufficiently describe FLK-2 receptor. On page 5 of the Office Action, the Examiner states that “[t]he instant claims do not provide sufficient structural and functional characteristics coupled with a known or disclosed correlation between function and structure.” Applicants disagree and assert that the specification provides an adequate written description of FLK-2 receptor.

Written description is sufficient when “the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed.” MPEP § 2163.02. The applicant shows possession “by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention.” *Id.* In this case, the specification discloses the structural and functional limitations that characterize the FLK-2 receptors claimed by the inventor.

The specification provides the structure of FLK-2 receptors and the correlation between structure and function. In the specification at page 6, lines 25-32 “the complete cDNA and amino acid sequences of the human flk-2 receptor” are provided. Next, the Applicants correlate each portion of the primary structure of the receptor to its corresponding function: “Amino acids -27 to -1 constitute the hydrophobic leader sequence. Amino acids 1 to 516 constitute the extracellular receptor domain. Amino acids 517 to 536 constitute the

transmembrane region. Amino acids 537 to 966 constitute the intracellular catalytic domain.” This description also provides information about the tertiary structure of the receptor and how the receptor is positioned within a membrane.

The specification provides a structural and functional description of the “FLK-2 receptor” genus. The Applicants describe a representative number of receptors falling within the scope of the genus at pages 11-12 of the specification. The Applicants also describe the structure and function of the class as a whole. At page 11, lines 6-15, the Applicants describe the characteristic domains and their corresponding functions independent of the sequences of particular species.

In addition to identifying the structural characteristics of the FLK-2 receptor genus, the Applicants also describe the expression and activity of the genus. The specification at page 9, lines 24-29 describes the expression and activity of the class of claimed receptors. The Applicants set forth “particularly strongly conserved residues and sequences” at page 8 of the specification. With the guidance from page 8 of the specification, one skilled in the art would know which sequences are essential to the invention.

For these reasons, the specification provides an adequate written description of FLK-2 receptor. To further clarify the FLK-2 receptor, Applicants have amended claim 81 to recite a specific sequence for FLK-2, SEQ ID NO:2 or SEQ ID NO:4. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Enablement

Claim 81 has been rejected under 35 U.S.C. § 112, first paragraph for failure to provide enablement for any FLK-2 receptor. The Examiner explains that the “Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-Terminal sequence, etc.) that distinctly identifies the scope of ‘FLK-2 receptor’.” The Examiner reiterates that the specification does not “provide sufficient written description as to the structural features of any ‘FLK-2 receptor’ and the correlation between the chemical structure and the function of the genus of ‘FLK-2 receptors’.” Applicants

disagree and assert that the specification enables one of ordinary skill in the art to make and use the claimed method for any FLK-2 receptor.

The enablement requirement is met when the specification contains sufficient information to enable one of ordinary skill in the art to make and use the claimed invention. MPEP § 2164.01. One of ordinary skill in the art must be able to practice the invention with reasonable, not undue, experimentation. *Id.* There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue.” *See* MPEP § 2164.01(a). These factors include, but are not limited to: the breadth of the claims; the nature of the invention; the state of the prior art; the level of one of ordinary skill; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and, the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *See id.* It is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. *See id.* The examiner’s analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. *See id.*

The specification discloses sufficient biochemical information to identify any FLK-2 receptor. The class of FLK-2 receptors is characterized by “easily found domains” as described in the specification at page 11, lines 6-15. The Applicant sets forth the amino acid composition of the class of FLK-2 receptors by listing strongly conserved residues and sequences at page 8 of the specification. By setting forth the characteristic domains and characteristic conserved sequences of FLK-2 receptors, the Applicants have enabled one of ordinary skill in the art to practice the claimed method for any FLK-2 receptor. Once the FLK-2 receptor is described, one of ordinary skill in the art would understand how to make and use antibodies specific for that receptor.

The disclosure of strongly conserved sequences addresses the Examiner’s concern that one of ordinary skill in the art must have “knowledge of and guidance with regard to which amino acids in the polypeptide’s sequence, if any, are tolerant of modification and which are

conserved (i.e. expectedly intolerant to modification).” Page 8 of the specification discloses the conserved sequences so that one of ordinary skill in the art can predict which changes can be tolerated in a FLK-2 receptor. Thus, the sequences of the class of FLK-2 receptors is predictable in view of the specification, and one of ordinary skill in the art could identify the class of FLK-2 receptors with only reasonable experimentation.

For these reasons, the specification enables one of ordinary skill in the art to make and use the claimed method for any FLK-2 receptor. Applicants respectfully request that this rejection be withdrawn.

Indefiniteness

Claim 81 has been rejected under 35 U.S.C. § 112, second paragraph for indefiniteness. The Examiner explains that the applicant fails to “particularly point out and distinctly claim the ‘FLK-2 receptor’ by claiming sufficient characteristics associated with the protein (e.g., activity, molecular weight, amino acid composition, N-terminal sequence, etc.).” Applicants disagree and assert that the specification particularly points out the characteristics of an “FLK-2 receptor”.

When other elements of patentability are satisfied, the Examiner “should allow claims which define the patentable subject matter with a reasonable degree of particularity and distinctness. Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire.” MPEP § 2173.02. Definiteness of claim language is determined by whether one of ordinary skill in the art can “interpret the metes and bounds of the claim so as to understand how to avoid infringement.” *Id.* One of ordinary skill in the art reading the specification of the present application would understand that the term “FLK-2 receptor” is a receptor that embodies the structure and performs the activity described in the specification.

The Examiner states that the recitation of “FLK-2 receptor” is indefinite “because it is not clear whether the claimed specificity is ‘FLK-2’ or a ‘receptor of FLK-2’.” The

specification at page 5 lines 28-33 disclose that a FLK-2 is a receptor. Thus, "FKL-2 receptor" is simply a more descriptive term for the same polypeptide.

As discussed above, the specification discloses the structure and function of the FLK-2 receptors. Applicants direct the Examiner to the above discussion regarding the disclosure of the activity and amino acid sequence of the FLK-2 receptor. The specification provides the structural and functional limitations of term FLK-2 receptor. These limitations set forth the metes and bounds of the invention, and thus provide notice to others of what constitutes infringement.

Moreover, Applicants have amended claim 81 to recite an extracellular portion of a protein tyrosine kinase that is FLK-2, wherein the extracellular portion defined by amino acids 1-517 of SEQ ID NO:2 or defined by amino acids 1-516 of SEQ ID NO:4. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Obviousness

Claim 81 has been rejected under 35 U.S.C. § 103(a) as rendered obvious by Tsukamoto et al. (USPN 5,061,620) in view of Matthews et al. (Cell 65: 1143-1152, 1991) (1449). Applicants have amended claim 81 to recite the specificity of the antibody for the extracellular portion of FLK-2 encoded by SEQ ID NO:2 or SEQ ID NO:4.

Applicants submits that the Office has not set forth a *prima facie* case of obviousness. To establish *prima facie* obviousness, *inter alia*, the prior art references, when combined, must teach or suggest all the claim limitations, there must be some suggestion or motivation to combine the reference teachings and a reasonable expectation of success. MPEP § 2143.

The present invention provides a method for isolating cells that express FLK-2 receptors on their surface. The cells may be isolated by binding the cells to an antibody specific for the FLK-2 receptor and separating those cells bound to the antibody. Matthews does not disclose or suggest the particularly sequences of the claimed method, nor does Tsukamoto cure this deficiency. Accordingly, the references fail to motivate one of skill in

Appl. No. 09/919,408
Amdt. dated Dec. 2, 2003
Reply to Office Action of June 2, 2003

the art to make the present invention. The invention is, thus, not obvious in view of the cited references and this rejection under 35 U.S.C. § 103(a) should be withdrawn.

Appl. No. 09/919,408
Amdt. dated Dec. 2, 2003
Reply to Office Action of June 2, 2003

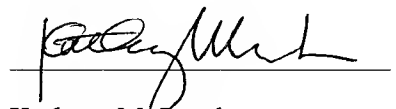
CONCLUSION

Applicants believes that the present application is in condition for allowance, and respectfully request that the Office pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

Dated: December 2, 2003

By:


Kathryn M. Lumb
Reg. No. 46,885
KENYON & KENYON
One Broadway
New York, New York 10004
(212) 908-6277 (telephone)
(212) 425-5288 (facsimile)

CUSTOMER NO. 26646